

Cancel Claims 1-35

36. (new) A method for diagnosing pregnancy-related complications in a pregnant woman comprising:

(a) providing PP13-responding cells having a membrane;

5 (b) exposing said cells to standard PP13;

(c) exposing PP13-responding cells to PP13 obtained from said woman, the cells of step (c) being:

i) other than the cells of step (b) or

10 ii) the same as the cells of step (b), but after sufficient washing to remove the standard PP13;

(d) determining the existence of a modification in the permeability of the cell membrane in (b) and in (c) as a result of exposure to PP13; and

15 (e) comparing the modification in permeability in (b) and (c), a change in the permeability of (c) as compared to the permeability in (b) indicating the existence of a pregnancy complication in said woman.

20 37. (new) A method according to Claim 36 wherein the modification in membrane permeability is determined by measuring cell membrane depolarization.

38. (new) A method according to Claim 37 wherein the cell membrane depolarization is measured using a cell membrane electrode or a voltage-sensitive dye.

25 39. (new) A method according to Claim 36 wherein the modification in membrane permeability is determined by measuring inward ion current.

40. (new) A method according to Claim 39 wherein the inward ion current is measured using a cell membrane electrode or a current-sensitive dye.

41. (new) A method according to Claim 36 wherein the modification in membrane permeability is determined by measuring calcium influx.
42. (new) A method according to Claim 41 wherein the calcium
5 influx is measured using a cell membrane electrode, a calcium-sensitive dye or radio-labeled calcium ions.
43. (new) A method according to Claim 36 wherein said pregnancy-related complication is intrauterine growth retardation (IUGR).
- 10 44. (new) A method according to Claim 36 wherein said PP13-responding cells are selected from the group consisting of primary cultured trophoblasts, immortalized trophoblast cell lines and placental organ culture.
45. (new) A method according to Claim 36 wherein said PP13
15 obtained from said woman is in a form selected from the group consisting of:
- a. a purified preparation from body fluids;
 - b. PP13-encoding DNA isolated from the woman and expressed in host cells or in a cell-free
20 preparation; and
 - c. after purification from the placenta.
46. (new) A method according to Claim 45 wherein purification from the placenta is selected from the group of maternal placenta derived primary cultures, chorionic vilouse
25 sampling (CVS) or their derived placenta tissue cultures or cultured trophoblasts and miscarriage or abortion tissues.
47. (new) A method according to Claim 36 wherein the membrane permeability is measured quantitatively with reference to
30 a dose response curve prepared using PP13 standards.

48. (new) A kit for diagnosing pregnancy complications in a pregnant woman comprising:
- a. PP13 standards; and
 - b. a dye selected from a voltage sensitive dye, a calcium sensitive dye and a current sensitive dye.
49. (new) A kit according to Claim 48 further comprising a calcium chelator and/or calcium blocker preparation.
50. (new) A method for diagnosing pregnancy-related complications in a pregnant woman comprising:
- a. providing a membrane phospholipid suspension;
 - b. exposing a first portion of said suspension to standard PP13;
 - c. exposing a second portion of said suspension to PP13 obtained from said woman;
 - d. determining the level of hydrolysis of the phospholipids to free fatty acids in (b) and (c); and
 - e. comparing the level of hydrolysis in (b) and (c), a change in the level of hydrolysis of (c) as compared to the level of hydrolysis in (b) indicating the existence of a pregnancy-related complication in said woman.
51. (new) A method according to Claim 50 wherein said membrane phospholipid suspension is selected from the group consisting of:
- a. isolated or cell culture membranes;
 - b. a cell-free biological phospholipid preparation; and
 - c. a cell-free artificial phospholipid preparation.
52. (new) A method according to Claim 50 wherein the level of hydrolysis is determined by determining the release of free fatty acids.

53. (new) A method according to Claim 50 wherein said fatty acids are arachidonic acids (AA) and/or linoleic acids (LA).
54. (new) A method according to Claim 50 wherein said pregnancy-related complication is IUGR and/or preeclampsia.
55. (new) A kit for diagnosing pregnancy-related complications in a pregnant woman comprising:
- a. PP13 standards;
 - b. fatty acid standards; and, optionally,
 - c. developing reagents to detect free fatty acids and/or their derivatives.
56. (new) A kit according to Claim 55 wherein said fatty acid standards are selected from the group consisting of LA and AA.
57. (new) A method for the differential diagnosis of pregnancy-related complications in a pregnant woman comprising tests which measure cell membrane depolarization, inward current, calcium influx, and LA and AA amounts, and wherein:
- a. a low amount of linoleic acid while all other tests are normal indicates a condition of mild (type I) IUGR;
 - b. a low amount of linoleic acid and arachidonic acid, low depolarization and calcium current and normal inward current indicates a condition of severe (type II) IUGR;
 - c. a low amount of linoleic acid and a high amount of arachidonic acid, while all other tests are normal indicates a condition of mild (type I) preeclampsia;

- d. a low amount of arachidonic acid, while all other tests are normal indicates a condition of severe (type II) preeclampsia;
 - e. all tests give low results indicates a condition of combined IUGR and preeclampsia; and
 - f. all tests are normal indicates the pregnancy is normal.
58. (new) A method for diagnosing pregnancy-related complications in a pregnant woman comprising:
- a. providing a membrane phospholipid suspension;
 - b. exposing a first portion of said suspension to standard PP13;
 - c. exposing a second portion of said suspension to PP13 obtained from said woman;
 - d. measuring the production of prostaglandins in (b) and (c); and
 - e. comparing the amounts of prostaglandins produced in (b) and (c), a change in the amount of prostaglandins of (c) as compared to the amount of prostaglandins in (b) indicating the existence of a pregnancy-related complication in said woman.
59. (new) A method according to Claim 58 wherein said prostaglandins are prostacyclin (PCN) and/or thromboxane (THX).
60. (new) A method according to Claim 58 wherein said prostaglandin is PCN and said pregnancy-related complication is preeclampsia, and the amount of PCN found in step 31(c) is significantly lower than found in 31(b).
61. (new) A method according to Claim 58 wherein:
- a. a low amount of PCN and a normal amount of THX indicates a condition of mild (type I) IUGR;

- b. a low amount of PCN and a low amount of THX indicates a condition of severe (type II) IUGR;
 - c. a low amount of PCN and a high amount of THX indicates a condition of mild (type I) preeclampsia;
 - 5 d. a normal amount of PCN and a high amount of THX indicates a condition of severe (type II) preeclampsia;
 - e. low amounts of PCN and THX indicate a condition of combined IUGR and preeclampsia; and
 - 10 f. normal amounts of PCN and THX indicate the pregnancy is normal.
62. (new) A measuring apparatus for use in diagnosing pregnancy-related complications in a pregnant woman, the apparatus comprising:
- 15 a. a measuring unit operable to measure modifications in the permeability of the membrane of PP13-responding cells and generate measured data indicative thereof; and
 - b. a control unit having:
 - 20 i. a memory utility for storing reference data indicative of normal modification in the permeability of the membrane of a PP13-responding cell as a result of exposure to standard PP13; and
 - 25 ii. a data processing utility pre-programmed to be responsive to measured data obtained by using PP-13 obtained from a pregnant woman, for processing said measured data by comparing it with the reference data, and generating output
 - 30 data indicative of a difference between them,

Preliminary Amendment: Attachment A

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Page 7

thereby enabling diagnosis of pregnancy-related complications.